PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference W 4494-007	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/SE2004/000328	International filing date *(day/month/year)* 05.03.2004	Priority date *(day/month/year)* 05.03.2003
International Patent Classification (IPC) or national classification and IPC A61L24/02		
Applicant BONE SUPPORT AB et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04.10.2004	30.08.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Schnack, A Telephone No. +49 89 2399-8149

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE2004/000328

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-27	as published
Claims, Numbers	
1-45	as published
Drawings, Sheets	
1/3-3/3	as published

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
   - ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
   - ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

   see separate sheet

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 39-45

   because:

   ☒ the said international application, or the said claims Nos. 39-45 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

   ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

   ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

   ☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	12-16
	No:	Claims	1-11, 17-45
Inventive step (IS)	Yes:	Claims	none
	No:	Claims	1-45
Industrial applicability (IA)	Yes:	Claims	1-38
	No:	Claims	see separate sheet.

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

The following documents were cited in the international search report:

D1: WO 02 05861 A1
D2: EP-A1-0 639 382
D3: NILSSON M. ET AL.: 'Characterization of a novel calcium phosphate/sulphate bone cement' J. OF BIOMEDICAL MATERIALS RESEARCH vol. 61, no. 4, 2002, pages 600 - 607, XP002229751
D4: MIRTCHI A.A. ET AL.: 'Calcium phosphate cements: action of setting regulators on the properties of the beta-tricalcium phosphate-monocalcium phosphate cements' BIOMATERIALS vol. 10, November 1989, pages 634 - 638, XP002949444
D5: BOHNER M. ET AL.: 'Effects of sulfate ions on the in vitro properties of beta-TCP - MCPM - water mixtures. Preliminary in vivo results' CERAMIC TRANSACTIONS vol. 48, 1995, pages 245 - 259, XP002949443
D6: WO 04 000374 A1
D7: BOHNER M.: 'New hydraulic cements based on alpha-tricalcium phosphate-calcium sulfate dihydrate mixtures' BIOMATERIALS vol. 25, 2004, pages 741 - 749, XP004471066
D8: WO 03 053488 A1
D9: WO 03 041753 A1

Section II
Priority
The presently claimed priority right appears to be valid.

Section III
Non-establishment of opinion
Claims 39-45 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Section V
V.1. Novelty

Remarks under Article 33(3) PCT:

The present invention relates to an injectable bone mineral substitute material composition with the capacity of being hardened in a body fluid in vivo. The object of the invention is to provide a composition which hardens in a body fluid in vivo during surgery; which provides a stable lasting implant over a year with high mechanical strength; which does not exhibit the drawbacks of high viscosity at delivery and which has excellent biocompatibility as well as favourable biological and rheological properties.

The claimed composition comprises at least one calcium phosphate component and at least one calcium sulphate component as a dry mixture with an aqueous liquid, and at least one accelerator, the at least one calcium sulphate being particulate hardened calcium sulphate, which has a specified particle size that confers injectability to the composition.

D1 discloses a composition of the claimed type, which comprises a calcium phosphate and a calcium sulphate component as a dry mixture mixed with an aqueous liquid, and at least one accelerator. The calcium phosphate is preferably tricalcium phosphate and the calcium sulphate is preferably calcium sulphate hemihydrate, but according to claim 24 of D1, up to 95% of the hemihydrate can be replaced by hardened calcium sulphate dehydrate in order to improve the injectability. The particle size of the calcium sulphate hemihydrate or dehydrate should preferably be 1-10 µm (see claims 2 of D1).

The subject matter according to present claims 1-11 and 17-45 thus lacks novelty in view of D1.

V.2. Inventive step

Remarks under Article 33(3) PCT:

D2 discloses an injectable bone mineral substitute material comprising a plastic substance mixed with crystalline ceramic calcium phosphate, which includes a non-ionic X-ray contrast aid, preferably Iohexol, (see claim 1-4).

D1 is considered to constitute the closest prior art. The subject matter according to present

claims 14-16 differ from D1 in that the disodium hydrogen phosphate is included in the calcium sulphate component, whereas in D1 it is dissolved in the liquid component. There is no evidence on file that this difference gives rise to a technical effect in a non-obvious manner. These claims are therefore considered to lack an inventive step.

The subject matter according to present claims 12-13 and 39-41 differs from D1 in that a water-soluble non-ionic X-ray contrast agent is included in the composition. The technical effect of this difference is that the X-ray density of the bone substitute is increased. Additionally, the decline in X-ray density when the water-soluble agent disappears can be used to monitor the healing process. However, from D2 it is already known to include a water-soluble X-ray contrast agent in the ceramic part of a bone substitute material. Thus, the person skilled in the art, having the bone substitute material according to D1 as the starting point, aiming to solve the identified problem, would with the knowledge of D2 include such an agent into the composition, and thus arrive at the invention according to present claims 12-13 and 39-41. Thus, these claims appear to be devoid any inventive teaching.

V.3. Industrial applicability
Remarks under Article 33(4) PCT:

For the assessment of the present claims 39-45 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VI
Certain documents
The intermediate documents D6-D9 may become relevant in the subsequent national/regional phase.

Section VIII
Certain defects
Remarks under Article 5 and 6 PCT:
The subject matter according to claims 42-45 should be amended so as to claim the use of the compositions according to the independent product claim 1.